Treatment intensification with insulin glargine in patients with inadequately controlled type 2 diabetes improves glycaemic control with a high treatment satisfaction and no weight gain

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Abstract: PRINCIPLES: We aimed to evaluate the efficacy of, and treatment satisfaction with, insulin glargine administered with SoloSTAR® or ClikSTAR® pens in patients with type 2 diabetes mellitus managed by primary care physicians in Switzerland. METHODS: A total of 327 patients with inadequately controlled type 2 diabetes were enrolled by 72 physicians in this prospective observational study, which aimed to evaluate the efficacy of a 6-month course of insulin glargine therapy measured as development of glycaemic control (glycosylated haemoglobin [HbA1c] and fasting plasma glucose [FPG]) and weight change. We also assessed preference for reusable or disposable pens, and treatment satisfaction. RESULTS: After 6 months, the mean daily dose of insulin glargine was 27.7±14.3 U, and dose titration was completed in 228 (72.4%) patients. Mean HbA1c decreased from 8.9%±1.6% (n=327) to 7.3%±1.0% (n=315) ($p<0.0001$), and 138 (43.8%) patients achieved an HbA1c 7.0%. Mean FPG decreased from 10.9±4.5 to 7.3±1.8 mmol/l ($p<0.0001$). Mean body weight did not change (85.4±17.2 kg vs 85.0±16.5 kg; $p=0.11$). Patients' preference was in favour of the disposable SoloStar® pen (80%), as compared with the reusable ClickStar® pen (20%). Overall, 92.6% of physicians and 96.3% of patients were satisfied or very satisfied with the insulin glargine therapy. CONCLUSIONS: In patients with type 2 diabetes insulin glargine administered by SoloSTAR® or ClikSTAR® pens, education on insulin injection and on self-management of diabetes was associated with clinically meaningful improvements in HbA1c and FPG without a mean collective weight gain. The vast majority of both patients and primary care physicians were satisfied with the treatment intensification.

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Treatment intensification with insulin glargine in patients with inadequately controlled type 2 diabetes improves glycaemic control with a high treatment satisfaction and no weight gain

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Summary

PRINCIPLES: We aimed to evaluate the efficacy of, and treatment satisfaction with, insulin glargine administered with SoloSTAR® or ClikSTAR® pens in patients with type 2 diabetes mellitus managed by primary care physicians in Switzerland.

METHODS: A total of 327 patients with inadequately controlled type 2 diabetes were enrolled by 72 physicians in this prospective observational study, which aimed to evaluate the efficacy of a 6-month course of insulin glargine therapy measured as development of glycaemic control (glycosylated haemoglobin [HbA_{1c}] and fasting plasma glucose [FPG]) and weight change. We also assessed preference for reusable or disposable pens, and treatment satisfaction.

RESULTS: After 6 months, the mean daily dose of insulin glargine was 27.7 ± 14.3 U, and dose titration was completed in 228 (72.4%) patients. Mean HbA_{1c} decreased from 8.9% ± 1.6% (n = 327) to 7.3% ± 1.0% (n = 315) (p <0.0001), and 138 (43.8%) patients achieved an HbA_{1c} ≤7.0%. Mean FPG decreased from 10.9 ± 4.5 to 7.3 ± 1.8 mmol/l (p <0.0001). Mean body weight did not change (85.4 ± 17.2 kg vs 85.0 ± 16.5 kg; p = 0.11). Patients' preference was in favour of the disposable SoloStar® pen (80%), as compared with the reusable ClickStar® pen (20%). Overall, 92.6% of physicians and 96.3% of patients were satisfied or very satisfied with the insulin glargine therapy.

CONCLUSIONS: In patients with type 2 diabetes insulin glargine administered by SoloSTAR® or ClikSTAR® pens, education on insulin injection and on self-management of diabetes was associated with clinically meaningful improvements in HbA_{1c} and FPG without a mean collective weight gain. The vast majority of both patients and primary care physicians were satisfied with the treatment intensification.

Key words: *type 2 diabetes mellitus; insulin glargine; ClikSTAR®; SoloSTAR®; HbA_{1c}; FPG; patient satisfaction; patient empowerment; primary care*

Introduction

Diabetes mellitus represents a fast growing worldwide epidemic: In 2010, an estimated 285 million people were affected by type 2 diabetes. The projected numbers for 2030 reach 439 million people, owing to a marked increase of prevalence in young adults and adolescents and, in certain regions such as Africa, the Middle East and Asia [1]. In Switzerland, the prevalence of type 2 diabetes is estimated at 5.7–7% of the overall population, corresponding to approximately 500,000 people [2]. In patients with type 2 diabetes, hyperglycaemia enhances the risk of vascular disease, acute myocardial infarction, stroke, lower limb amputation and microvascular complications [2–6]. Real-life data from a survey in 157,000 American patients with type 2 diabetes, however, indicate that over two-thirds of the patients have HbA_{1c} concentrations >6.5%, which may cause considerable long-term complications and healthcare costs [7].

Once life-style intervention and one or more oral antidiabetic drugs (OADs) become ineffective to lower HbA_{1c} to target levels, the addition of basal insulin, particularly in patients with high fasting blood glucose (FBG) levels, is highly recommended [8]. Good glycaemic control over time is required to reduce the risk of diabetes-associated complications [8, 10]. Type 2 diabetes guidelines and algorithms that highlight the importance of basal insulin for the management of the disease have been published in recent years jointly by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Based on the above mentioned guidelines, the SSED (Swiss Society of Endocrinology and Diabetes) has published its own recommendations [12, 13]. Whereas the addition of basal insulin to existing OAD treatment was

recommended in patients with HbA_{1c} levels above 7% in the former SSED guidelines from 2009 [12], individual target levels between 6% and 8% are recommended in the new SSED guidelines published in 2013 [13].

Clinical trials demonstrated the benefit of insulin glargine, a basal-insulin analogue [14], to achieve HbA_{1c} levels of <7% in patients with uncontrolled type 2 diabetes mellitus [8, 15–27]. Optimisation and long-term maintenance of glycaemic control with insulin glargine was confirmed in large cohorts of patients with type 2 diabetes [10, 22, 23], and advantages of insulin glargine compared with other insulins and antidiabetic medication were described in several studies [8, 15, 17, 19, 20, 24, 25].

Patients requiring insulin are challenged by complex interventions for their disease. They have to manage multiple blood glucose measurements and to balance carbohydrate intake and daily insulin injections [8]. Failure to initiate or noncompliance with insulin treatment regimens represents a common and critical issue for reaching therapeutic goals. Insulin use by patients is often limited by factors such as fear of injection and hypoglycaemia, but could also be also related to the injection device itself. Therefore, easy-to-use devices may positively influence physicians' insulin prescribing habits and patient compliance [8]. The convenient and simple handling of SoloSTAR® and ClikSTAR® represents a big step forward towards easy self-management of diabetes and lead to increased treatment adherence and higher patient satisfaction [8, 26]. Thus, administration of insulin glargine with SoloSTAR® and ClikSTAR® pens contributes to the optimisation of diabetes treatment [27].

In addition, education on self-management of diabetes reflects a further important aspect of the current patient-centred approach. The later focuses on the patient's needs and abilities with the aim to improve their knowledge and skills, thus enabling better self-management of treatment regimens and life-style interventions [8, 28, 29].

The aim of the present study was to evaluate the efficacy of a 6-month course of insulin glargine therapy measured as development of the glycaemic control (HbA_{1c} and FPG) and weight change. We also assessed, whether patients will choose a reusable or a disposable pen, and the treatment satisfaction with SoloSTAR® (disposable pre-filled insulin pen) and ClikSTAR® (reusable insulin pen for 3 ml insulin cartridges) in patients with type 2 diabetes mellitus managed by primary care physicians in various regions of Switzerland.

Patients and methods

Patients

Seventy-two physicians in primary medical care across Switzerland participated in the present prospective observational study conducted between November 2009 and September 2011. All patients with poorly controlled type 2 diabetes mellitus despite prior treatment with OAD(s) or insulin were eligible to participate. Inclusion criteria were age >18 years, HbA_{1c} >7%, and the patient's informed consent. There were no exclusion criteria. The reasons for nonparticipation in the study were not systematically captured. In accordance with local regulations, informed consent was provided by the participating patients. Treatment with insulin glargine (Lantus®, Sanofi-Aventis (Schweiz) AG, Vernier, Switzerland) and pens for subcutaneous administration (SoloSTAR® and ClikSTAR®, Sanofi-Aventis (Schweiz) AG, Vernier, Switzerland) was prescribed as a part of routine medical care and used according to the product information [30]. Participating physicians were encouraged to provide education on the appropriate administration of insulin glargine, the use of pens and concomitant life-style interventions to enable patients to self-manage their disease and to assist patients to choose which pen to use (the disposable (SoloSTAR) or the reuseable (ClikSTAR) pen). Information on self-management of diabetes was at the discretion of the treating physician. The first patient was included in the observation study on 1 November 2009 and the last patient was included on 31 March 2011. With the exception of the first visit and a visit at after 6 months of insulin glargine treatment, there was no systematic monitoring of treatment with insulin glargine other than routine clinical visits as ordered by the participating physicians. The study was approved by an Independent Ethics Committee according to local regulations.

Outcome measures

Patient demographics, vital signs (systolic and diastolic blood pressure) and lipids (triglycerides, high and low density lipoprotein cholesterol), medical history and complications of diabetes, concomitant diseases, previous treatment of diabetes, and recommended dose titration of insulin glargine were recorded at the baseline (BL) visit. Initial dose, titration scheme and actual dose of insulin glargine were recorded at the follow-up (FU) routine medical care visit after 6 months. The effectiveness parameters (HbA_{1c} and FPG) were recorded at the BL and FU visits. There was no reference laboratory used for the biochemical analysis, but rather the laboratory in the doctor's office or an external laboratory used by the doctor's office. Safety events were reported directly to the Swissmedic Pharmacovigilance centres according to national regulatory requirements. Satisfaction was evaluated using the four-point Likert scale (very dissatisfied, dissatisfied, satisfied, very satisfied) by interview of the patients and by questionnaire for the physicians. The results were entered into the case report form (CRF) directly by participating physicians.

Statistical analysis

All patients with data records at BL and FU visits were included in the intention-to-treat (ITT) analysis (n = 315), and all patients compliant with the eligibility criteria and appropriate visit interval were considered for the per-protocol (PP) analysis (n = 300). Baseline characteristics, antidiabetic treatment and safety were assessed in the ITT population. Efficacy (HbA_{1c} and FPG) and treatment satisfaction were analysed using the PP population. Continuous variables with a normal distribution were described as means with standard deviations (SDs), and group comparisons were performed with the independent or paired t-test; continuous variables with a skewed distribution were presented as median values. Changes in HbA_{1c} between different titration groups was analysed by using multiple linear regression, controlled for baseline HbA_{1c} with and

Bonferroni-correction of the significance level if more than two groups were compared. Discrete variables were presented as frequencies and percentages, and group comparisons were performed using the chi-square test. All reported p-values are two-sided. Patient data were entered into the CRF directly by the treating physicians. Data management and analysis was performed by Ulrich Kreuter Statistik GmbH, Schwarzenburg. Data were analysed using SAS 9.1, SAS Institute Inc., SAS Campus Drive, Cary, North Carolina 27513, USA.

Results

Patient disposition

Out of 327 patients included, 12 (3.7%) patients did not return to the FU visit and were considered as lost to follow-up. In 9 (2.8%) out of 315 patients (ITT) early termination due to intermittent disease, patient's decision, noncompliance or short visit interval (<8 weeks) was recorded. Furthermore, 6 (1.9%) patients with HbA_{1c} <7.0% at the BL visit (representing a protocol violation) were excluded from the PP population (300 patients). The mean number of patients enrolled per centre was 4.4 (median 4). With regard to the distribution across regions, all major areas and language regions of Switzerland were represented in

Table 1: Demographics, blood pressure, lipids, medical history (mean ± SD) and diabetic complications (No. and %) at the baseline visit (intention to treat population, n = 315).

Demographics	**No.**	**Mean**	**Standard deviation**
Gender: Female	147 (46.7%)		
Male	168 (53.3%)		
Age (years)	315	62.2	11.4
Weight (kg)	315	85.4	17.2
Height (cm)	315	161.1	16.3
Body mass index (kg/m^2)	315	29.7	5.4
Smoking (% of study population)	314	85 (27.1)	
Blood pressure			
Systolic blood pressure (mm Hg)	309	139.4	14.2
Diastolic blood pressure (mm Hg)	309	83.1	9.4
Lipids			
Triglycerides (µmol/l)	215	2.52	1.36
High density lipoproteins (µmol/l)	210	1.18	0.62
Low density lipoproteins (µmol/l)	199	3.23	1.13
Medical history			
Diabetes duration (years)		7.26	6.28
Diabetic complications (micro- and macro-vascular)		**No.**	**%**
Retinopathy	315	38	12.1
Nephropathy	315	67	21.3
Known microalbuminuria	315	106	33.7
Neuropathy	315	66	21.0
Coronary heart disease	315	82	26.0
--- Myocardial infarction	82	29	35.4
Stroke	315	5	1.6
Peripheral arterial occlusive disease	315	22	7.0

Table 2: Use of antidiabetic drugs prior to enrolment and reasons to change the antidiabetic treatment indicated at baseline visit. Figures represent the number and percent of patients in the intention to treat population (n = 315).

(a) Previous treatments					
Oral antidiabetics	282	89.5%	**Insulin**	47	14.9%
Metformin	259	82.2%	Short-acting	11	3.5%
Sulfonylurea	126	40.0%	Intermediate-acting	19	6.3%
Glitazones	100	31.7%	Long-acting	30	9.5%
Glinides	27	8.6%			
GLP-1 agonists	3	1.0%			
DPP-4 Inhibitors	53	16.8%			
(b) Reasons to change treatment					
Oral antidiabetics	282	89.5%	**Insulin**	47	14.9%
Not on target	230	81.6%	Not on target	35	74.5%
Hypoglycaemia	5	1.8%	Hypoglycaemia	9	19.1%
Skin irritation	9	3.2%	Skin irritation	2	4.3%
Other adverse events	21	7.4%	Other adverse events	1	2.1%
Dissatisfaction	30	10.6%	Dissatisfaction	1	2.1%
			Pen	1	2.1%

DPP-4 = dipeptidyl peptidase-4; GLP-1 = glucagon-like peptide-1

this study: 244 (77.5%) patients were included from the German-speaking, 39 (12.4%) from the French-speaking, and 32 (10.1%) from the Italian-speaking parts of Switzerland.

Demographics and disease characteristics

Baseline characteristics are presented in table 1. The mean age (±SD) was 62.2 ± 11.4 years (range 17–92 years) and the mean body mass index (BMI) was 29.7 ± 5.4 (range 17–56). The mean systolic and diastolic blood pressures were 139 ± 14 and 83 ± 9 mm Hg, respectively, the mean concentrations of triglycerides (TG), high density lipoprotein (HDL) and low density lipoprotein (LDL) cholesterol were 2.52 ± 1.36 µmol/l, 1.18 ± 0.62 µmol/l and 3.23 ± 1.13 µmol/l, respectively. The average time from the diagnosis of diabetes was 7.3 ± 6.3 years and the following diabetic complications were reported at baseline: microalbuminuria (33.7%), coronary heart disease (26.0%) including myocardial infarction in 9.2%), peripheral arterial occlusive disease (7.0%), stroke (1.6%), neuropathy (21.3%), nephropathy (21.0%) and retinopathy (12.1%). In total, 27.0% of patients were smokers.

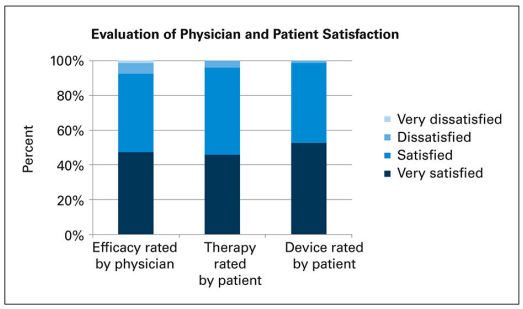

Figure 1

Assessment of efficacy (blood glucose control) by physician, evaluation of satisfaction with therapy and device by patients: Proportions of physicians and patients who were “very satisfied”, “satisfied”, “dissatisfied” or “very dissatisfied” (per protocol population, n = 300).

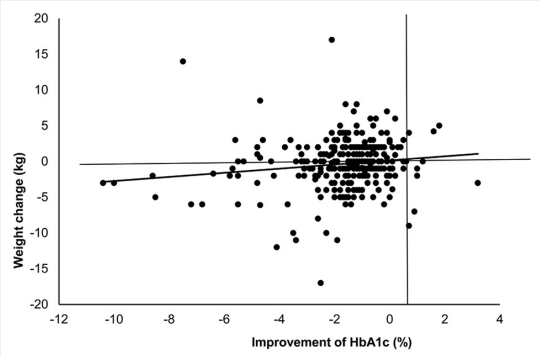

Figure 2

Weight change in relation to improvement of HbA_{1c}. Correlation of weight change and change in HbA_{1c}, p = 0.01.

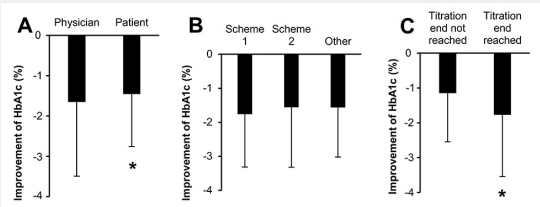

Figure 3

Improvement of HbA_{1c} with the different titration schemes.
A) Physician = titration managed by physician (n = 221), patient = titration managed by patient (n = 91); p = 0.049, adjusted for baseline HbA_{1c}.
B) Improvement of HbA_{1c} in the different titration groups. 1 = change of 2 U every 3 days (n = 58), 2 = weekly adjustment (n = 230), 2 = other titration scheme (n = 27), p = not significant, adjusted for baseline HbA_{1c}.
C) Titration end not reached (n = 87), Titration end reached (n = 228); p <0.001, adjusted for baseline HbA_{1c}.

Treatments

At the BL visit, 282 (89.9%) patients were treated with one or more OADs and 47 (14.9%) patients with insulin. The proportions of patients using metformin, sulfonylureas, glitazones, DPP-4–inhibitors, glinides, GLP-1–agonists and any insulin are shown in table 2a. Sulfonylureas were prescribed initially to 126 (40.0%) patients and at 6 months to 87 patients (27.6%), of whom 5 had a dose reduction, and 3 were additionally started on sulfonylureas. The reasons to change OAD or insulin treatment are summarised in table 2b.

Titration of insulin glargine and therapeutic education of patients

The initial dose of insulin glargine was either 10 U (61.9%) or 0.2 U/kg (26.7%) according to protocol, and in 11.4% of the patients the initial insulin dose was higher (mean ± SD 16.5 ± 8.6 U), mostly in patients that were previously on insulin treatment. The titration of glargine was managed by physicians (71.1%) or by patients (28.9%), either with weekly adjustment (73.0%) or a change of 2 U every 3 days (18.4%), and was completed at the FU visit after 6 months in 72.4% of the patients. These patients had a lower HbA_{1c} level as compared with the patients not finishing titration (fig. 3C). The insulin dose was adjusted according to two established algorithms, which could be chosen by the physician: Once weekly, based on the FPG values during the two previous days (table 3) or, more simply, an increase of 2 U every three days, if the FBG was not on target. The titration scheme was not associated with a different HbA_{1c} (fig. 3B). However, titration by the physician resulted in a slightly higher HbA_{1c} improvement as compared with titration by the patient (fig. 3A). The mean daily dose of insulin glargine was 27.7 ± 14.3 U and the mean duration of treatment was 178 ± 56 days. ClickSTAR® and SoloSTAR® pens were used in 20% and 80% of patients, respectively. The proportion of patients treated with OADs remained stable during the study period (89.9% at BL vs 88.9% at the FU visit).

At the BL visit, education on self-management of diabetes was carried out in 303 (96.2%) patients, mainly by physicians (95.4%), diabetes experts (37.3%), diet experts (28.1%) and psychotherapists (1.0%). A similar pattern of educational support was recorded at the FU visit.

Efficacy

In the ITT population, the mean HbA_{1c} decreased from 8.9% ± 1.6% at the BL visit to 7.3% ± 1.0% at the FU visit, resulting in a significant difference of –1.6% ± 1.7% (p <0.0001). The mean FPG decreased from 10.8 ± 4.4 mmol/l at the BL visit to 7.3 ± 1.8 mmol/l at the FU visit with a significant change of –3.6 ± 4.5 mmol/l (p <0.0001). The proportion of patients with an HbA_{1c} level ≤7.0% increased from 4.8% to 43.8% (p <0.0001), and the proportion of patients with FPG ≤7.0 mmol/l increased from 9.6% to 50.3% (p <0.0001). The mean body weight remained stable during the study period (85.4 ± 17.2 kg at the BL vs 85.0 ± 16.5 kg at the FU visit; p = 0.11).

In the PP population, the mean HbA_{1c} decreased from 8.9% ± 1.6% at the BL visit to 7.3% ± 1.0% at the FU visit resulting in a significant difference of –1.6% ± 1.7% (p <0.0001) (table 4). At the BL visit, the mean HbA_{1c} correlated significantly (p = 0.022) with age group, being the highest (9.5% ± 1.8%) in patients ≤49 years and the lowest (8.6% ± 1.4%) in patients ≥ 70 years. The differences from the BL visit to the FU visit showed a trend (p = 0.19) to greatest prominence in the youngest compared with the oldest age, resulting in a similar mean HbA_{1c} at the FU visit (table 4c). The mean FPG decreased from 10.9 ± 4.5 mmol/l at the BL visit to 7.3 ± 1.8 mmol/l at the FU visit with a significant change of –3.6 ± 4.6 mmol/l (p <0.0001). The proportion of patients with an HbA_{1c} level ≤7.0% increased from 3.0% to 45.3% (p <0.0001), and the proportion of patients with FPG ≤7.0 mmol/l increased from 9.2% to 50.7% (p <0.0001). The mean body weight remained stable during the study period (85.4 ± 17.2 kg at BL vs 85.0 ± 16.5 kg at the FU visit; p = 0.11) (fig. 2).

Tolerability

At the beginning of this prospective observational study, participating physicians were informed about their obligation to report spontaneous serious safety events directly to the Swissmedic Pharmacovigilance centres using the specific Swissmedic form. Hypoglycaemia was reported in one (0.3%) patient in the comment section of the CRF. Otherwise, no adverse drug reactions have been documented.

Outcomes assessments and patient satisfaction

Overall, 92.7% of treating physicians and 96.3% of patients were satisfied or very satisfied with the insulin glargine therapy (fig. 1); 45.3% physicians and 50.3% patients were satisfied whilst 47.3% physicians and 46.0% patients were very satisfied with the insulin glargine therapy. Similarly, 99.0% of patients were satisfied or very satisfied with the use of SoloSTAR® or ClikSTAR® pens; 46.3% patients were satisfied and 52.7% were very satisfied with the SoloSTAR® or ClikSTAR® pens. The patients' preference was in favour for the disposable SoloSTAR® pen (80%), as compared with the reusable ClickSTAR® pen (20%).

Discussion

In this prospective, observational study conducted in a large cohort of patients with previously uncontrolled type

Table 4: (a) Mean (standard deviation; SD) HbA1c and fasting blood glucose (FPG) at baseline (BL) and follow-up (FU) visits. The paired differences in mean (SD) HbA1c and FPG from BL visit to FU visit after 6 months. The reported p-values were calculated using the paired t-test. (b) Number and frequency of patients allocated to defined groups of HbA1c and FPG levels at BL and FU visits. (c) Mean (SD) HbA1c by age group at BL and FU visits and mean change from BL visit to FU visit after 6 months. Figures represent the number and percent of patients of the per protocol population (n = 300).

(a) Mean values	**Visit**	**No.**	**Mean**	**SD**	**95% confidence interval**	**p-value**
HbA_{1c} (%)	BL	300	8.9	1.6	8.7–9.1	
	FU	300	7.3	1.0	7.1–7.4	
Difference	FU – BL	300	-1.6	1.7	1.8–1.5	<0.0001
FPG (mmol/l)	BL	295*	10.9	4.5	10.4–11.4	
	FU	294*	7.3	1.8	7.0–7.5	
Difference	FU – BL	293*	–3.7	4.6	4.2–3.1	<0.0001
(b) Distribution	**Visit**	**No.**	**≤6.5%**	**≤7.0%**	**≤8.0%**	**>8.0%**
HbA_{1c} (%)	BL	300	0 (0.0%)	9 (3.0%)	97 (32.3%)	194 (64.7%)
	FU	300	63 (21.0%)	73 (24.3%)	122 (40.7%)	42 (14.0%)
			≤5.5	**≤7.0**	**≤8.0**	**>8.0**
FPG (mmol/l)	BL	295*	4 (1.4%)	23 (7.8%)	38 (12.9%)	230 (78.0%)
	FU	294*	37 (12.6%)	112 (38.1%)	78 (26.5%)	67 (22.8%)
HbA_{1c} by age group	**Visit**	**Age group**	**No.**	**Mean**	**SD**	**p-value**
HbA_{1c} (%)	BL	≤49	35	9.5	1.8	
		50–59	77	9.1	1.9	
		60–69	108	8.8	1.4	
		≥70	80	8.6	1.4	0.022
HbA_{1c} (%)	FU	≤49	35	7.5	0.9	
		50–59	77	7.2	0.9	
		60–69	108	7.2	0.8	
		≥70	80	7.2	1.1	0.49
HbA_{1c} (%)	FU – BL	≤49	35	–2.1	1.9	
		50–59	77	–1.8	2.1	
		60–69	108	–1.6	1.3	
		≥70	80	–1.4	1.6	0.19

* Lower numbers are due to missing values.

2 diabetes mellitus in a primary care setting, a 6-month course of insulin glargine administered with SoloSTAR® or ClikSTAR® pens, and education on insulin injection with these devices and on self-management of diabetes was associated with a clinically relevant improvement in glycaemic control (fasting plasma glucose and HbA_{1c}) without an increase in mean body weight of the entire cohort. The vast majority of patients and physicians were satisfied with the treatment.

Comparison of randomised studies with real world results of this observational study

Our study presents "real world" results of a patient-centred approach encompassing treatment with insulin glargine using ClickSTAR® and SoloSTAR® pens and education by physicians to enable patients to self-manage the disease. Initiation of insulin glargine treatment and dose titration was managed in 73% of patients according the scheme of Riddle et al. [15] and in 18% of patients following the scheme of the ADA/EASD [11]. Interestingly, self-management of dose titration was reported more frequently in the present study than in a previous study [22] conducted between 2005 and 2007 in Switzerland (29% vs 17%). This observation mirrors a trend in the medical community to increasingly promote therapeutic education and self-empowerment of patients. However, our results demonstrate that titration by the physician resulted in a slightly higher improvement of HbA_{1c}, in contrast to the choice of titration scheme, which did not influence the outcome. The titration was completed after 6 months in 72% of patients with a mean insulin glargine dose of 27.7 ± 14.3 U, corresponding to a mean of 0.32 ± 0.17 U/kg. This resembles the lower range of insulin replacement in patients with initial treatment intensification. The patients who completed the titration scheme had a significantly lower HbA_{1c} level.

In agreement with results from large clinical trials [15, 17, 20, 21], treatment with insulin glargine during a period of 24 weeks resulted in a clinically relevant decrease in HbA_{1c} and FPG. Surprisingly, despite a marked improvement in glycaemic control, body weight remained stable during the treatment period in our study, which supports the argument that weight gain is not always a complication of insulin treatment, particularly when using not very high insulin doses.

The SSED guidelines of 2009 [12], which applied when the study started, recommended an HbA_{1c} target level of ≤7.0%, and the current SSED guidelines [13] recommend an individual target level of 6% to 8%, whereas for most of the patients a value of ≤7.0% is still desirable nowadays. In our study, 45% of patients achieved an HbA_{1c} level of ≤7.0%. The mean HbA_{1c} level after 6 months treatment with insulin glargine was 7.3% ± 1.0% and was similar across all age groups. A similar response rate was observed in previous studies [20, 21], whereas response rates between 60% to 77% were reported elsewhere [15, 22].

Recent studies (ACCORD, ADVANCE und VADT) [32–34] resulted in the new joint recommendations from the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) [8] with individual aims for HbA_{1c} of higher than <7% in patients with pre-existing cardiovascular complications, long duration of diabetes and a history of hypoglycaemia. During our study these recommendations [8] were not yet available. The ideal HbA_{1c} range now recommended is between 6%–7.5% with the lowest complications at an HbA_{1c} of 6.5% for microvascular and 7% for macrovascular complications. Only for a short diabetes duration without cardiovascular complications and without frequent hypoglycaemia is an HbA_{1c} of <7% still recommended. Aggressive treatment with an HbA_{1c} target of ≤6.5% was shown to have an increased risk of mortality, probably because of hypoglycaemia. In our study, the median duration of diabetes was 6.2 years (and a large proportion of patients already had cardiovascular disease at the time of enrolment, suggesting a study population at high risk for cardiovascular events). We did not analyse individual patient's HbA_{1c} targets, but obviously, many physicians chose a less stringent target in patients with a longer duration of the disease even before the new recommendations were published. Otherwise, the proportion of patients in whom the dose titration was deemed to be completed would have been higher than 72%.

Table 3: Weekly insulin titration schedule based on self-measured fasting blood glucose (FBG) [15].

Average FBG during the past 2 days	Change in insulin dose (U/day)
≥10 mmol/l	8
7.8–9.9 mmol/l	6
6.7–7.7 mmol/l	4
5.6–6.6 mmol/l	2
4.5–5.5 mmol/l	0
<4.5 mmol/l	–2

Limitations of the study

The absence of any further safety information represents the major limitation of this study, in particular the lack on hypoglycaemic events. Since this is a prospective observational study, serious adverse events such as hypoglycaemia have to be reported directly to Swissmedic Pharmacovigilance centres and can, therefore, not be analysed. One single report of hypoglycaemia, considered to be non serious was recorded by a physician as a comment in the CRF. The fact that no more comments on serious events were reported in the CRF, could be for various reasons: (a) an indication that the primary care physicians adopted a less aggressive and therefore safe titration method, or (b) patients chose a lower insulin dose than prescribed by the physician or suggested by the algorithm scheme, as documented by the low mean insulin dose at the end of follow-up of 28 units, which corresponds to only nine titration steps by two units, whereas 26 or 60 steps would have been possible according to the two different titration algorithms suggested. There was no systematic monitoring of insulin glargine treatment during the 6-month observation other than routine clinical visits at baseline and at the end of the study period. The fact that no reference laboratory was involved and the participating physicians used their own arrangements for measuring blood sugar parameters represents a limitation of the study because of potential differences in measurement methods and bias, but it will most likely not affect the calculated differences. Since the HbA_{1c} at baseline was 8.9% in the present study, we considered it unethical not

to give insulin in this group of patients with a long diabetes duration. Therefore, the study lacks a direct comparison group. Although we have included more than 300 patients treated by 72 different physicans from all three major language regions of Switzerland, further studies in randomised populations would be needed before the results can be applied to the wider type 2 diabetes population in Switzerland.

Treatment satisfaction

As in a previous study [22], the vast majority of treating physicians and patients were satisfied or very satisfied with the insulin glargine therapy. It is interesting that 80% of patients chose a disposable pen for initial insulin treatment. In addition, 99% of patients were satisfied or very satisfied with use of the SoloSTAR® or ClikSTAR® pens in the present study. The preference for disposable pens and the satisfaction underlines the simplicity of education in the handling of these devices and their acceptance by the patients.

Whereas randomised comparative trials reflect a methodical approach with defined patient populations, systematic data collection and head-to-head comparisons of treatments, "real life" outcomes generated in observational studies provide insights into day-to-day medical practice in unselected patient populations.

In conclusion, treatment with insulin glargine administered with SoloSTAR® or ClikSTAR® pens and education on insulin injection with these devices and on self-management of diabetes was associated with clinically meaningful improvements in HbA_{1c} and fasting plasma glucose without a mean collective weight gain during a 6-month study period in patients with type 2 diabetes mellitus, who has previously failed to reach local targets under OAD treatment. In primary care practice, this treatment offers good glycaemic control at a stable body weight, thus contributing to a high satisfaction of both patients and treating physicians.

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Authors' contribution: DR and DS contributed equally.

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Figures (large format)

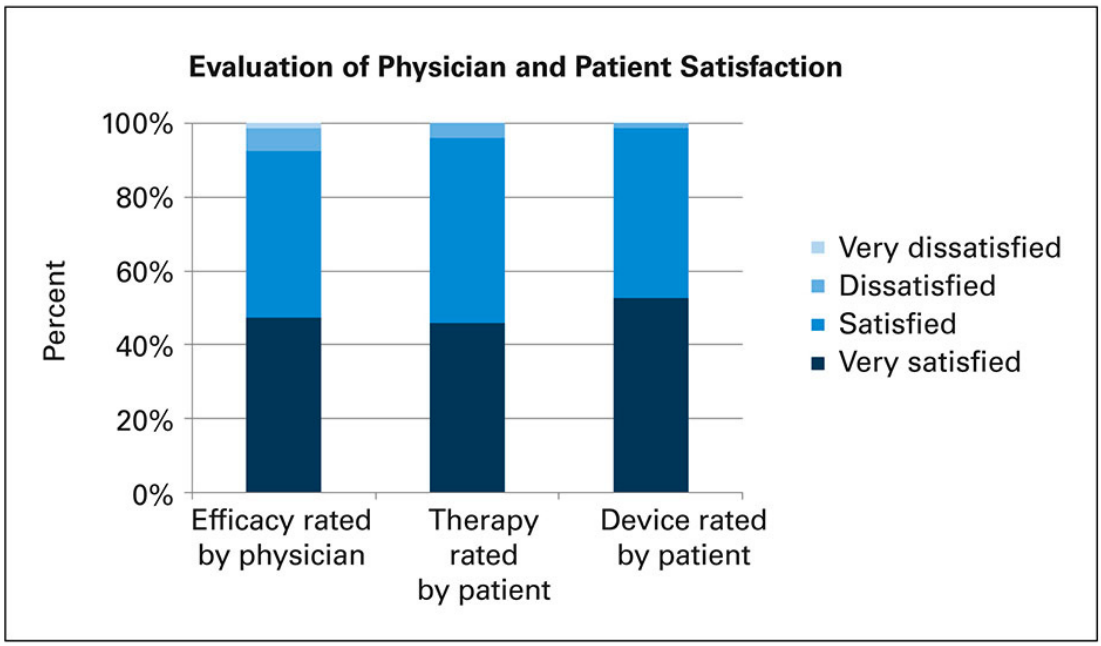

Figure 1

Assessment of efficacy (blood glucose control) by physician, evaluation of satisfaction with therapy and device by patients: Proportions of physicians and patients who were “very satisfied”, “satisfied”, “dissatisfied” or “very dissatisfied” (per protocol population, n = 300).

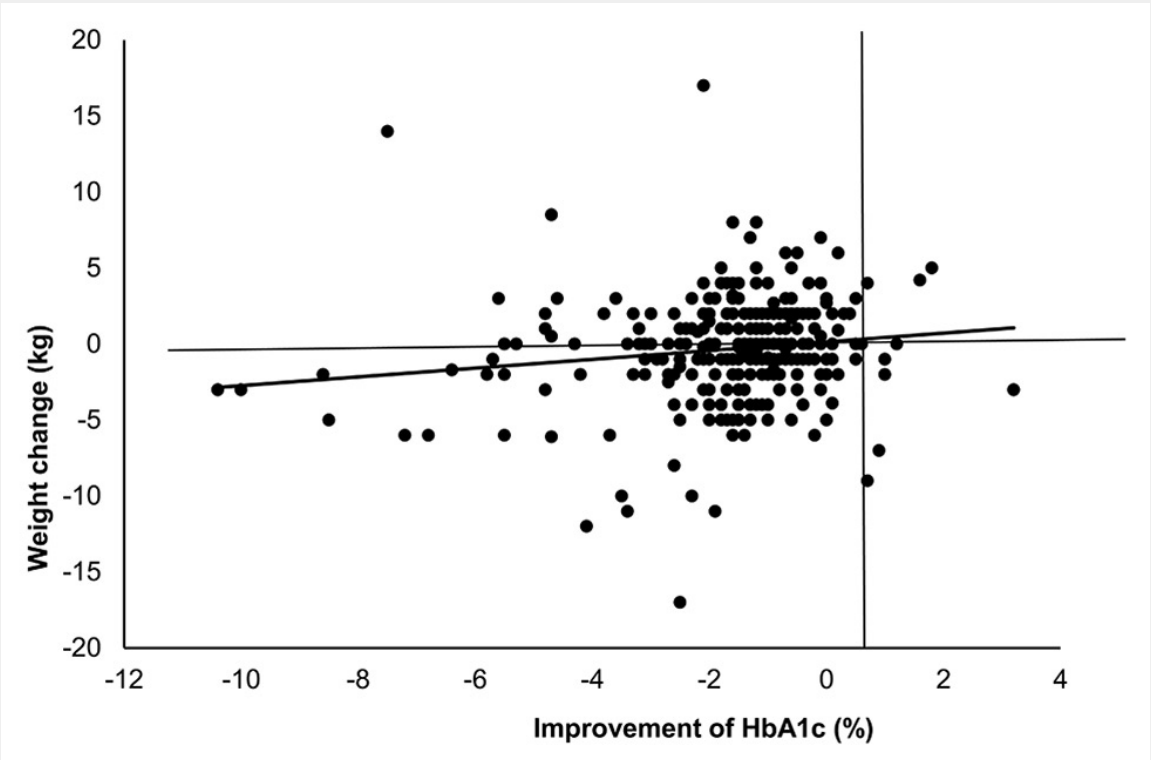

Figure 2

Weight change in relation to improvement of HbA_{1c}. Correlation of weight change and change in HbA_{1c}, p = 0.01.

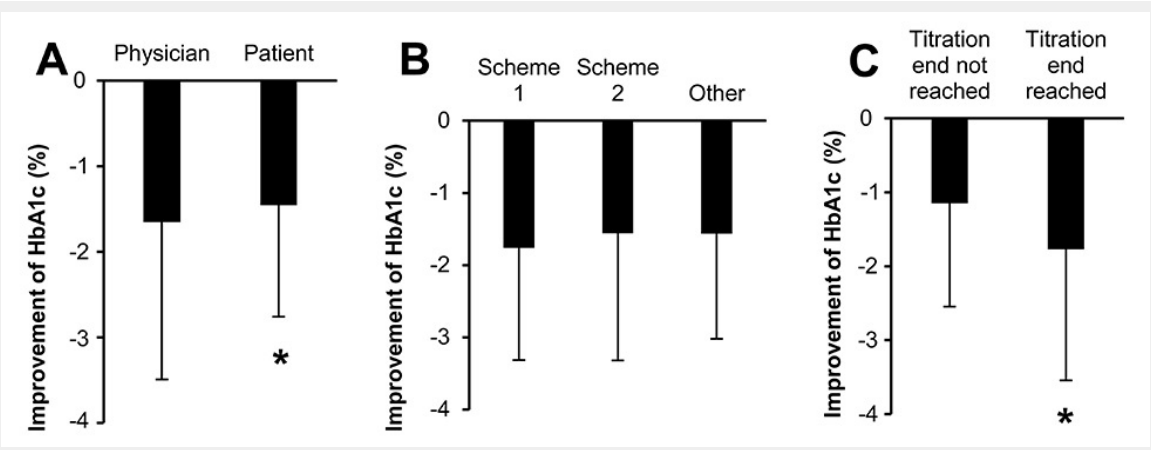

Figure 3

Improvement of HbA_{1c} with the different titration schemes.

A) Physician = titration managed by physician (n = 221), patient = titration managed by patient (n = 91); p = 0.049, adjusted for baseline HbA_{1c}.

B) Improvement of HbA_{1c} in the different titration groups. 1 = change of 2 U every 3 days (n = 58), 2 = weekly adjustment (n = 230), 2 = other titration scheme (n = 27), p = not significant, adjusted for baseline HbA_{1c}.

C) Titration end not reached (n = 87), Titration end reached (n = 228); p <0.001, adjusted for baseline HbA_{1c}.